REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.114, are respectfully requested.

By the foregoing amendment, claim 21 has been amended to recite "chronic cardiac dysfunction . . . ." Support for the amendment to claim 21 can be found throughout the originally filed application including, for instance, page 2, lines 15-23; page 4, lines 25-34; and page 21, line 25 – page 22, line 2. Thus, no new matter has been added.

Turning now to the Office Action, the Examiner has rejected claims 8-11 and 21 under 35 U.S.C. § 112, first paragraph, because the specification supposedly does not enable treatment of cardiac hypertrophy with ANP in species other than rates at dosages which do not cause diuretic and hypotensive effects and do not teach treatment of cardiac hypertrophy with agents other than ANP at dosages which do not cause diuretic and hypotensive effects. This rejection is respectfully traversed.

To be enabling under § 112, a patent application must contain a description that enables one skilled in the art to make and use the claimed invention. That some experimentation is necessary does not preclude enablement. The amount of experimentation simply must not be unduly extensive. *See, e.g., Atlas Powder Co. v. E. I. DuPont de Nemours & Co.*, 224 U.S.P.Q. 409, 413 (Fed. Cir. 1984).

The Examiner is of the view that the subject to be treated should be limited to rat. Applicants respectfully disagree with the Examiner's view. Under United States practice, a pharmacological experimental result obtained by rat or other experimental result obtained by rat or other experimental animal can support treatment of other subjects including human.

For example, in the Blaine et al. patent, Example 11, which is the sole pharmacological experiment, does not define the animal used. In a pharmacological experiment, information on the animal used is essential. Therefore, the content of Example 11 in the Blaine et al. patent (the same patent which the Examiner utilized in the anticipation rejection discussed below and there must consider to be enabling as a reference cannot be used as prior art unless it is enabling) is weaker than the experiment of the present application. Nevertheless, in the Blaine et al. patent, method claims without animal limitation have been allowed. If the same criterion applied to the Blaine et al. patent is applied to the present invention, the method claims without animal limitation should be allowed.

In addition, the Examiner stated on page 5 of the Office Action, that the same animal was used in the Blaine et al. patent and the present invention. In the present invention, rat was used. This means that the Examiner deemed that rat was used in the Blaine et al. patent. If this is the case, in the Blaine et al. patent, method claims without animal limitation on the basis of experiment using rat were allowed.

The Federal Circuit has indicated that *in vivo* testing in humans is not a requirement for satisfying the requirements of 35 U.S.C. § 112, first paragraph. *See, e.g., In re Brana*, 34 U.S.P.Q.2d 1437, 1442-43 (Fed. Cir. 1995). Here, the Examiner has not met his initial burden of providing evidence or scientific reasoning that the disclosed rat models are insufficient to support the claimed method for treating humans. Rather, by utilizing the Blaine et al. patent in an anticipation rejection, the Examiner has implicitly admitted that applicants' claimed invention is enabling without limitation on the basis of experiments using rats. Additionally, as set forth in applicants' previous response filed on February 19, 2004,

applicants have provided sufficient evidence to establish the validity of the rat hypercardia model for human treatment as well.

Regarding the scope of active component, the specification of the present invention shows that any substance which was activity to increase cGMP activity via GC-A receptors is useful. In addition, the specification describes a method for selection of the above-mentioned active substance. Furthermore, the specification lists ANP and BNP, and BNP increases cGMP activity. Therefore, if the usefulness of AP was proved, it is reasonably considered that BNP and other substances activating cGMP via CG-A receptor should be useful.

About 1988 to 1989, prior to the priority date of the present application, regarding natriuretic peptide receptors, genes for three receptors had been known, and the relationship between receptors and ligands had been clarified (Fuller et al., J. Biolo. Chem. 1988:263:9395; Chinkers M. et al., Nature 1989:338:78; Schulz S. et al. Cell 1989:58:11155). On the basis of such findings, the relationship between ligands and receptors was clarified, and it was clarified that ANP and BNP are endogenous ligands for GC-A (for example, Nakao K. et al., J. Hypertens. 1992:10:907). After that and so far, other receptors have not been found. Therefore, it is believed that in all mammals, ANP and BNP exhibit their biological activities via GC-A.

Therefore, a person with ordinary skill in the art would consider that human ANP, rat ANP, and BNP of various animals, as well as other natriuretic derivatives exhibit ANP-like biological activity corresponding to affinity to GC-A or agonist activity. Therefore, such substances should be useful for the present invention.

In view of the above, the Examiner is respectfully requested to withdraw the enablement rejection pursuant to 35 U.S.C. § 112, first paragraph.

Furthermore, the Examiner has rejected claims 8-11 and 21 under 35 U.S.C. § 102(b) as allegedly being anticipated by Blaine et al. (U.S. Patent No. 4,652,549) as evidence by Espiner. This rejection is respectfully traversed.

Initially, it is noted that the Examiner has indicated that this rejection was being reinstated "[i]n view of [the] amendment to the claims removing the claim language requiring removal of pulmonary congestion to be the causative effect . . . ." Applicants do not fully understand the Examiner's argument and thus request further explanation in this regard.

Nevertheless, for prior art to be anticipatory, every element of the claimed invention must be disclosed in a single item of prior art in the form literally defined in the claims. *See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986). Regarding the instant rejection, the Blaine et al. patent does not refer to treatment of chronic cardiac dysfunction. As such, the Blaine et al. patent, either alone or evidenced by Espiner, does not anticipate the claimed invention.

In view of the above, the Examiner is respectfully requested to with this anticipation rejection under 35 U.S.C. § 102(b).

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this Amendment and Reply, or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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